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PREMARKET NOTIFICATION [510(k)] SUMMARY

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Contact Person: Dr Roberto Liddi
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Date: 23rd October 2002

Device Name: Cozart RapiScan

Trade Name: Cozart RapiScan Oral Fluid Drug Test System–
Opiate/Methadone

Classification Name: Methadone Test System
Opiate Test System

Classification: Class II
Code of Federal Regulations Title 21 Food and Drugs
Part 862 Clinical Chemistry and Clinical Toxicology
Devices
Subpart D Clinical Toxicology Test Systems
Section 862.3620 Methadone Test System
Section 862.3650 Opiate Test System

Establishment Registration No.: 3002336046

Performance Standards: BS EN ISO 9001:1994, EN 46001:1996

Substantial Equivalence: RapidOne Opiates Test, 510(k) no. k971961
RapidOne Methadone Test, 510(k) no. k992325

Introduction

The Cozart RapiScan Oral Fluid Drug Test System for Opiates and Methadone is a point of care test (POCT) for the detection of both opiates and methadone in human oral fluid using cutoffs of 40 and 30 ng/mL respectively, in neat oral fluid. The performance of the Cozart RapiScan opiates and methadone test was compared to GC/MS. Cozart Bioscience Ltd is the manufacturer of the Cozart RapiScan Oral Fluid Drug Test System– Opiate/Methadone. We have not purchased this device from another manufacturer and the device is not marketed under another product name.

Intended Use

The Cozart RapiScan Oral Fluid Drug Test System - Opiates and Methadone is intended for Point of Care testing in a number of settings such as prescription workplace, drug dependency clinics, and criminal justice. It provides qualitative screening results for opiates and methadone in human oral fluid at a cut-off concentration equivalent to 40ng/mL and 30ng/mL respectively in neat oral fluid. The Cozart collection system involves a 1:3 dilution of the oral fluid sample, this dilution factor is corrected for in the Cozart RapiScan Drug Test and therefore the remainder of this document will refer to the cut-offs as 13ng/mL for opiates and 10ng/mL for methadone.

This kit has to be used in conjunction with the Cozart RapiScan instrument. Please refer to the sampling and testing procedures in the instructions for use leaflet.

This assay is for professional use only and provides only a preliminary analytical test result. Clinical consideration and professional judgement must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a more confirmed analytical result a more specific alternative chemical method is needed. Gas Chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method.

Where Used

The Cozart RapiScan opiates and methadone test is designed for point of care testing. All users of the test are trained by a Cozart representative, at the end of the training programme a certificate is issued.

Design and Materials

As can be seen from the Principle of the Test section in the package insert, the Cozart RapiScan opiates and methadone test system is a point of care test for the detection of opiates and methadone in human oral fluid.

The Cozart RapiScan opiates and methadone test system is composed of three parts – the oral fluid collection device, the opiates and methadone test cartridge and the Cozart RapiScan instrument.

1. Oral fluid Collection Device

This device is composed of an oral fluid collector pad, a transport tube containing run buffer and a dispense filter tube. The oral fluid collection pad is manufactured by Oral fluid Diagnostic Systems Inc, New York, USA. It is composed of a white plastic handle and a cellulose pad with a perforated edge. The white plastic handle incorporates a sample adequacy indicator, when 1mL of oral fluid has been collected the indicator in the handle turns blue.

The dispense filter tube pushes the sample pad down to the bottom of the transport tube and assists in mixing the oral fluid and buffer. The top of the tube is partially sealed incorporating a dropper dispense facility into the top. Six drops of the sample are added to the cartridge with the dispense filter tube.

2. Opiate and Methadone Test Cartridge

This is composed of a white reaction strip with immobilized drug sites for opiates and methadone contained in a blue plastic casing. The cartridge also has a pad containing gold labeled anti-morphine and gold labeled anti-methadone antibodies. In addition, the cartridge has a built in control line of sheep anti-mouse IgG antibody to ascertain that complete lateral transfer of specimen has been achieved. The opiate and methadone test cartridge is a single use device which should be disposed of after use.

3. Cozart RapiScan Instrument

The Cozart RapiScan instrument is a battery-powered instrument whose function is to automate the analysis of the opiate/methadone test cartridge. It is a hand-held low voltage optical scanner (complies with Electromagnetic Compatibility (EMC) Directive 89/336/EEC).

The cartridge is inserted into the machine for reading and is removed after the test has been read. Results are displayed on the screen as positive or negative. The Cozart RapiScan instrument must be used to read the cartridges, this eliminates the subjectivity of reading by eye.

The instrument is supplied with pre-printed non-disposable system test, positive QC and negative QC cartridges. The system test cartridge (labeled with SYS) is designed to test whether the instrument is functioning correctly. This should be performed at regular intervals throughout the use of the machine or when the instrument has been manhandled eg. dropped. The instrument displays SYSTEM TEST PASS or SYSTEM TEST FAIL on the screen of the instrument. The positive and negative QC cartridges (labeled with PQC and NQC) should be analysed at regular intervals in the same way as a test sample.

Performing the Test

A oral fluid sample is collected from the mouth by placing the sample pad under the tongue ensuring the pad is pointing downwards. This process can take from 1-10 minutes. Once the indicator in the sample pad has turned blue and 1mL of oral fluid has been collected the sample pad is removed from the mouth and placed into the transport tube. The pad is removed from the plastic handle along the perforated edge. The dispense filter tube is pushed into the transport tube purple end down until the sample pad is pushed to the bottom of the tube. The sample is then ready for testing.

The opiates and methadone test cartridge is removed from its foil pouch and placed on a flat surface. The transfer tube is carefully and very slowly inverted until it is horizontal. To add the sample, gently squeeze the end of the filter tube transferring 6 drops of sample into the cartridge. Once the liquid has appeared in the cartridge window, this takes between 2 and 60 seconds, the cartridge is then inserted into the Cozart RapiScan instrument. Pressing the start button initiates the timer to countdown 6 minutes after which the instrument automatically reads the cartridge and displays the results on the instrument screen. The results are displayed as positive or negative.

The Cozart RapiScan test cartridge and sample collection device are designed for use with the Cozart RapiScan instrument. The cartridges must be read with the instrument and not by eye. In addition to the quality control cartridges supplied with the instrument, other quality control specimens with known drug concentrations should be run through the test procedure following appropriate federal, state and local guidelines concerning the running of external quality controls. These are not supplied with the Cozart RapiScan opiates and methadone test system.

Interpreting the Result

The result is displayed on the screen of the Cozart RapiScan instrument as positive or negative. This means that the diluted sample has methadone or an opiate present. The dilution factor should be taken into consideration when interpreting the results, that is, 1mL of oral fluid is diluted in 2mL of Cozart RapiScan buffer (x3 dilution factor). 10ng/mL of methadone in a diluted sample will produce a positive result, this is equivalent to 30ng/mL in neat oral fluid. Similarly, 13ng/mL of morphine will produce a positive result, this is equivalent to 40ng/mL morphine in neat oral fluid. The test provides only a preliminary result and in order to obtain a more confirmed result Gas Chromatography/Mass Spectrometry (GC/MS) analysis should be performed.

Performance:

Method Comparison

The method comparison study using the Cozart RapiScan Opiates and Methadone test system was performed at Cozart Bioscience Ltd by Cozart Bioscience staff. The GC/MS was performed by FSS Chepstow UK, University of Glasgow, Scotland, and The Analytical Laboratory at Cozart Bioscience Ltd, UK.

A total of 454 Oral fluid samples were tested in the Cozart RapiScan Drug Test System according to the package insert.

99 samples from drug users enrolled at a drug rehabilitation clinic, were positive for opiates by the Cozart RapiScan System, of these samples 93 were confirmed positive by GC/MS. The GC/MS employs the set cut-off of 40ng/mL for Opiates in neat oral fluid.

124 samples were negative for opiates, 123 of these samples were confirmed negative by GC/MS. Of the negative samples 103 were from drug free volunteers, and the remaining 21 were from known drug users.

24 of all samples tested were within +50% to – 50% of the opiate cut-off. Of these, 14 had been previously diluted with blank saliva to give a concentration within the range of 60ng/mL to 20ng/mL.

116 samples from drug users enrolled at a drug rehabilitation clinic, were positive for Methadone by the Cozart RapiScan System and 116 were confirmed positive by GC/MS. The GC/MS employs the set cut-off of 30ng/mL for Methadone in neat oral fluid

115 samples were negative in the Cozart RapiScan System and were confirmed negative by GC/MS. 102 of these samples were from drug free volunteers, and the remaining 13 were from known drug users.

24 of all samples tested were within -50% to +50% of the methadone cut-off. Of these, 20 had previously been diluted with blank saliva to give a concentration within the range 45ng/mL to 15ng/mL.

Precision

Four oral fluid samples were tested in duplicate every day for twenty days. The samples were a negative, a negative sample spiked with drug at the cutoff concentration and negative samples spiked to 50% above and below the cutoff.

Acceptable results were obtained as can be seen in the table below:

<u>Opiate</u>	Opiate Concentration (ng/mL)			
	0	6.5	13	19.5
Positive	0	0	40	40
Negative	40	40	0	0

<u>Methadone</u>	Methadone Concentration (ng/mL)			
	0	5	10	15
Positive	0	0	40	40
Negative	40	40	0	0

To check whether the use of the Cozart RapiScan Drug Test System - Opiates/Methadone might be somehow influenced by a testing environment different from a laboratory setting, and by being used by untrained personnel, an extended Precision Study was conducted at 3 Point Of Care sites. Four oral fluid samples were collected from drug free volunteers and aliquots were fortified with Morphine and Methadone at the concentrations shown below just prior to onsite testing. The samples were tested up to 9 times for each site. The table below shows the results obtained.

<u>Opiate</u>	Opiate Concentration (ng/mL)			
	0	6.5	13	19.5
Positive	0	0	25	25
Negative	25	26	1	0

<u>Methadone</u>	Methadone Concentration (ng/ml)			
	0	5	10	15
Positive	0	0	24	23
Negative	25	26	2	2

Sensitivity

Eight negative oral fluid samples fortified with morphine and methadone at 50% above the cutoff concentration were serially diluted in increments of 25% of the cutoff concentration of the assay. The lowest concentration of drug detected above the detection cutoff is the detection limit. The detection limit for opiates is between 9.75ng/ml (-25% of the cut off value) and 6.5ng/ml (-50% of the cut off value) and for

methadone is between 7.5ng/ml (-25% of the cut off value) and 5ng/ml (-50% of the cut off value).

Specificity

The specificity can be defined as the extent to which related or unrelated compounds cross-react with the antibody employed in the assay. Twenty-eight potentially interfering substances were tested at 100,000ng/mL for cross-reactivity in the Cozart RapiScan opiates and methadone test and none were found to cross-react. Buprenorphine was tested at 10,000ng/mL due to the stock solution being at 100,000ng/mL.

The lowest concentration to produce a positive was determined for a number of related substances. Thirteen different members of the opiate family were tested – morphine, 6-monoacetylmorphine, codeine, dihydrocodeine, nalorphine, oxycodone, hydromorphone, hydrocodone, oxymorphone, norcodeine, pholcodine, heroin and morphine-3-glucuronide. Similarly, methadone and three of its metabolites were tested – 1- α -acetylmethadol (LAAM), 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), 2-ethylidene-5-methyl-3,3-diphenylpyrrolidine (EMDP). This experiment was carried out on three different batches of opiate/methadone test cartridges.

Cutoff Concentration

The cutoff concentration was determined by preparing 8 fortified oral fluid samples at the cutoff concentration, 50% above and below the cutoff concentrations and 100% above and below the cutoff concentrations. All the samples fortified at 50% below the cutoff were negative for both methadone and opiates. All the samples fortified at the cutoff concentration, 50% above and below the cutoff concentration and 100% above and below the cutoff concentration were positive for both opiates and methadone.

Interference Studies

A range of parameters including sample adequacy indicator dye, haemoglobin, smoking, coffee, tea, water, food, orange juice, hard candy, chewing gum and mouthwash were tested for interference in the Cozart RapiScan opiates and methadone test system. No interference was observed with any of the parameters.

Sample Stability

Samples were collected from volunteers, two were fortified with morphine and methadone at 50% above the cutoff and two were fortified with morphine and methadone at 50% below the cutoff concentration. The fortified samples and also two negative samples were then stored at both room temperature and 2-8°C and tested at day 0, 3, 7, 14, 21 and 28 in the Cozart RapiScan opiates and methadone test system. Samples are stable at both room temperature and 2-8°C for 28 days.

Freeze/Thaw Stability

Samples were collected from volunteers, two were fortified with morphine and methadone at 50% above the cutoff and two were fortified with morphine and methadone at 50% below the cutoff concentration. The fortified samples and also two negative samples were then subjected to six freeze/thaw cycles at -20°C before testing in the Cozart RapiScan opiates and methadone test system. Samples can undergo up to six freeze/thaw cycles prior to testing.

Time of Day Comparison

This experiment was designed to investigate whether sampling at different times of the day would have an effect on the results obtained with the Cozart RapiScan opiates and methadone test. Samples were collected from four volunteers at three different times of the day – morning, midday and evening. The morning sample was taken before breakfast, the midday sample was taken before lunch and the evening sample before bed. Each sample was then fortified with morphine and methadone at 50% above and below the cutoff concentration and tested. Sampling at different times of the day had no effect on the results obtained with the Cozart RapiScan opiates and methadone test system.

Instrument Comparison

This experiment was designed to investigate whether different instruments would produce different results with the Cozart RapiScan opiates and methadone test system. Samples were collected from four volunteers and spiked with morphine and methadone at 50% above and below the cutoff concentration then tested. All the testing was performed by a single operator with the same set of samples to ensure the only variable was the instrument. All three instruments produced unambiguous results.

Operator Comparison

This experiment was designed to ensure that the Cozart RapiScan opiates and methadone test system is not sensitive to operator effects. Samples were collected from four volunteers and fortified with morphine and methadone at 50% above and below the cutoff concentration. The samples were tested by inexperienced operators with the same instrument. The results for each sample were unambiguous for all three operators.

Accuracy/Recovery

Samples were collected from four volunteers and fortified with morphine and methadone at 50% above and below the cutoff concentration. This gave samples from four individuals at three concentrations – 0, 6.5 and 19.5ng/mL for morphine and 0, 5 and 15ng/mL for methadone. To these samples drug was added at 50% above and below the cutoff concentration, at the cutoff concentration and 100% above the cutoff concentration. The samples were tested in the Cozart RapiScan opiates and methadone test system. All samples were positive with the exception of the negative sample fortified with drug at 50% below the cutoff concentration as expected.

New Filter Tube

This experiment was designed to ensure that the sample testing volume from the new plunger. Previous testing showed that four drops from the old plunger were equal, on average, to six drops from the new plunger. Four different operators, weighted two sample each, one with the old system and one with the new system. This operation was repeated ten times. The balance used was a FX-40 AND Electronic balance [(d=0.0001g) serial no. 05704015], which is periodically calibrated according to Standard Operating Procedures. The results show no significant difference in weight between the two systems.

Chemical Safety

The sample collection contains Bovine Serum Albumin (BSA) obtained from a BSE free source. The cartridges are composed of a nitrocellulose membrane which may explode at high temperatures.

Human Factors

There are no human factors incorporated in any of the kit components.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 5 2002

Dr. Roberto Liddi
QA/RA Manager
Cozart Bioscience Limited
45 Milton Park
Abingdon
Oxfordshire, OX 14 4RU

Re: k020920
Trade/Device Name: Cozart RapiScan Oral Fluid Drug Test System – Opiate/Methadone
Regulation Number: 21 CFR § 862.3620 and 21 CFR § 862.3650
Regulation Name: Immunoassay, Methadone/ Immunoassay, Opiates
Regulatory Class: II
Product Code: DJR, DJG
Dated: October 3, 2002
Received: October 8, 2002

Dear Dr. Liddi:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

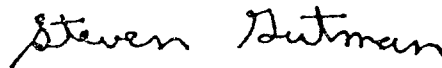
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, slightly slanted style.

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): k020920Device Name: Cozart RapiScan Oral Fluid Drug Test System- Opiate/Methadone

Indications For Use:

The Cozart RapiScan Oral Fluid Drug Test System - Opiates and Methadone is intended for Point of Care testing in a number of settings such as prescription workplace, drug dependency clinics, and criminal justice. It provides qualitative screening results for opiates and methadone in human oral fluid at a cut-off concentration equivalent to 40ng/mL and 30ng/mL respectively in neat oral fluid. The Cozart collection system involves a 1:3 dilution of the oral fluid sample, this dilution factor is corrected for in the Cozart RapiScan Drug Test and therefore the remainder of this document will refer to the cut-offs as 13ng/mL for opiates and 10ng/mL for methadone.

This kit has to be used in conjunction with the Cozart RapiScan instrument. Please refer to the sampling and testing procedures in the instructions for use leaflet.

This assay is for professional use only and provides only a preliminary analytical test result. Clinical consideration and professional judgement must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a more confirmed analytical result a more specific alternative chemical method is needed. Gas Chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method.

It is the responsibility of those organisations required to follow department of transportation (DOT) or the Substance Abuse and Mental Health Services Administration (SAMHSA) Workplace Drug Testing guidelines to determine that this product satisfies the criteria for workplace testing established under DOT and SAMHSA.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of GDRH, Office of Device Evaluation (ODE)

[Signature]
(Division Sign-Off)

Division of Clinical Laboratory

(Optional Format 3 10 98)

510(k) Number k020920

✓ Prescription and Prescription Workplace